

### **Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### **Listing of Claims:**

Claim 1 (currently amended): A device for the propagation of tissue comprising a bioartificial composite comprised of a substrate having at least one surface capable of the reception and growth promoting retention of a cellular preparation, and a first layer of adherent cells disposed on said surface, said first layer prepared from said cellular preparation, the cells comprising said first layer having cytoskeletal elements aligned substantially uniformly with an axis of the substrate, wherein said bioartificial composite acts as a template to accept a second layer of cells upon said first layer, said second layer comprising an organized layer of later-deposited cells oriented in the direction of said first layer, wherein said substrate has at least one surface defined by a critical surface curvature and/or a surface topography having non-uniform grooves substantially aligned with the axis of the substrate.

Claim 2 (original): The device of Claim 1 wherein said substrate has at least one cell accepting surface defined by an oriented surface roughness of at least 200 nm root mean squared.

Claim 3 (original): The device of Claim 1 wherein said substrate has at least one cell accepting surface defined by a surface curvature of equal or greater than  $.016 \text{ microns}^{-1}$ .

Claim 4 (cancelled)

Claim 5 (currently amended): The device of Claim 1 wherein said bioartificial composite possesses a substantially ~~an over all~~ non-planar shape.

Claim 6 (original): The device of Claim 1 wherein said substrate is coated with a biocompatible, growth promoting preparation, which preparation minimizes non-specific protein binding and optimizes attachment of said cells.

Claim 7 (original): The device of Claim 6 wherein said preparation is selected from the group consisting of surfactants, cell adhesion molecules, polycations, cell growth factors, and mixtures thereof.

Claim 8 (currently amended): A device for the preparation of implantable tissue comprising a bioartificial composite comprised of a substrate having at least one surface capable of the reception and growth promoting retention of a cellular preparation, and a first layer of adherent cells disposed on said surface, said first layer prepared from said cellular preparation, the cells comprising said first layer having cytoskeletal elements aligned substantially uniformly with an axis of the substrate, wherein said bioartificial composite acts as a template to accept a second layer of cells upon said first layer, said second layer comprising an organized layer of later-deposited cells oriented in the direction of said first layer, wherein said substrate has at least one surface defined by a critical surface curvature and[[/or]] a surface topography having non-uniform grooves substantially aligned with the axis of the substrate.

Claim 9 (original): The device of Claim 8 wherein said substrate has at least one cell accepting surface defined by an oriented surface roughness of at least 200 nm root mean squared.

Claim 10 (currently amended): The device of Claim 8 wherein ~~the said substrate has at least one~~ cell accepting surface is defined by a surface curvature of equal or greater than  $0.016 \text{ microns}^{-1}$ .

Claim 11 (cancelled)

Claim 12 (original): The device of Claim 8 wherein said bioartificial composite possesses an over all planar shape.

Claim 13 (original): The device of Claim 8 wherein said bioartificial composite possesses an over all non-planar shape.

Claim 14 (original): The device of Claim 8 wherein said substrate is coated with a biocompatible, growth promoting preparation, which preparation minimizes non-specific protein binding and optimizes attachment of said cells.

Claim 15 (original): The device of Claim 14 wherein said preparation is selected from the group consisting of surfactants, cell adhesion molecules, polycations, cell growth factors, and mixtures thereof.

Claim 16 (currently amended): The device of Claim 8 wherein said ~~bioartificial composite~~ substrate is defined by at least one filamentous element ~~substrate~~.

Claim 17 (currently amended): The device of Claim 8 wherein said ~~bioartificial composite~~ substrate is defined by at least one cylindrical element ~~substrate~~.

Claim 18 (original): The device of Claim 17 wherein said substrate has a diameter of less than 300  $\mu\text{m}$ .

Claim 19 (currently amended): The device of Claim 8 wherein said substrate ~~of said bioartificial composite further defines an axially aligned surface topography, and~~ is coated with cell attachment molecules; ~~and a~~ the first layer of cells being attached to said molecules, ~~which cells are adapted to undergo morphological rearrangement to align with the long axis of said substrate;~~ and ~~at least one~~ the second cell layer ~~[[of]] comprising different cells that have been attached to~~ [[the]] a free upper surface of said first layer, ~~which is also adapted to undergo the same said morphological rearrangement.~~

Claim 20 (currently amended): The device of Claim 19 wherein the ~~morphological rearrangement~~ substantially uniform alignment of the cytoskeletons of said first layer of cells which comprises the bioartificial composite is promoted and effected by the imposition of suitable force on said first layer and [[/or]] said substrate.

Claim 21 (currently amended): A method for the preparation of the substrate of the device of either of claims 1 or 8, which method comprises:

- a. preparing a suitable biomaterial as a three dimensional structure selected from sheets, strips, strands of indefinite length and fibers;
  - b. treating at least one outer surface of the biomaterial prepared in Step a. to form thereon at least one said surface for the reception of said first layer of cells;
  - c. recovering said treated biomaterial defining the said at least one surface of Step b.;
- wherein said biomaterial film of Step c. is adapted to serve as substrate for said device.

Claim 22 (withdrawn): A method for the preparation of a bioartificial composite useful for repair of tissues or organs in a host, said method comprising:

- a. preparing a substrate having a surface having the morphological characteristics of the desired tissues or organs said surface permitting the reception and growth promoting retention of a cellular preparation, wherein the cellular preparation comprises a quantity of cells capable of growth and aggregation to form a component of said tissues or organs;
- b. applying the cellular preparation to the surface of said substrate to form a first layer of adherent cells disposed on said surface having cytoskeletal elements aligned uniformly, wherein said first layer acts as a template to accept a second layer of cells upon said first layer, said second layer comprising an organized layer oriented in the direction of said first layer; and
- c. implanting the bioartificial composite of Step b. at the location of desired repair, whereby the growth of said tissue takes place in the host.

Claim 23 (withdrawn): The method of Claim 22 wherein said cellular preparation of Step b. is of a different cell type from that of said tissue.

Claim 24 (withdrawn): The method of Claim 22 wherein said cellular preparation of Step b. is genetically modified to deliver a therapeutic compound useful in the treatment of disease or the promotion of tissue repair.

Claim 25 (withdrawn): A method for the repair of damaged tissues or organs in a mammal comprising preparing a biological composite in accordance with the method of Claim 22.

Claim 26 (previously presented): A method for the preparation of tissue useful for repair of tissues or organs in a host, said method comprising:

a. preparing a substrate having a surface having the morphological characteristics of the desired tissue, said surface permitting the reception and growth promoting retention of a cellular preparation, wherein the cellular preparation comprises a quantity of cells capable of growth and aggregation to form said tissue;

b. applying the cellular preparation to the surface of Step a to form a first layer of adherent cells disposed on said surface having cytoskeletal elements aligned uniformly, wherein said first layer acts as a template to accept a second layer of cells upon said first layer, said second layer comprising an organized layer oriented in the direction of said first layer;

c. incubating the substrate of Step b. under conditions promoting the growth of said tissue thereon; and

d. recovering the tissue prepared in Step c.

Claim 27 (withdrawn): A method for the preparation of tissue useful for testing, development and discovery, said method comprising:

- a. preparing a substrate defining a surface having the following characteristics:
    - i. at least one cell accepting surface defined by an oriented surface roughness of at least 200 nm root mean squared;
    - ii. at least one cell accepting surface defined by a surface curvature of equal or greater than  $.016 \text{ microns}^{-1}$ ; and
    - iii. said substrate defines a repeating surface structure that enables cytoskeletal structures of cells applied thereto to become aligned uniformly;
  - b. applying to the surface of Step a. a cellular preparation, said cellular preparation comprising a quantity of cells capable of growth and aggregation to form a first layer of cells having uniformly-aligned cytoskeletal elements, the first layer being suitable to act as a template to accept a second layer of cells thereon and orient the second layer of cells in the direction of the first layer;
  - c. incubating the bioartificial product of Step b. with a different type of cell to effect growth of said tissue thereon; and
  - d. recovering the tissue prepared in Step c.;
- wherein said tissue may be used as a benchtop testing system or tissue surrogate.

Claim 28 (withdrawn): A method for the preparation of tissue useful for repair of tissues or organs in a host, said method comprising:

- a. preparing a substrate defining a surface having the following characteristics:
  - i. at least one cell accepting surface defined by an oriented surface roughness of at least 200 nm root mean squared;
  - ii. at least one cell accepting surface defined by a surface curvature of equal or greater than  $.016 \text{ microns}^{-1}$ ; and
  - iii. said substrate defines a repeating surface structure that enables cytoskeletal structures of cells applied thereto to become aligned uniformly;

- b. applying to the surface of Step a. a cellular preparation, said cellular preparation comprising a quantity of cells capable of growth and aggregation to form a first layer of cells having uniformly-aligned cytoskeletal elements, the first layer being suitable to act as a template to accept a second layer of cells thereon and orient the second layer of cells in the direction of the first layer;

- c. incubating the bioartificial product of Step b. with a different type of cell to affect growth of said tissue thereon; and d. recovering the tissue prepared in Step c;

wherein said tissue may be used for therapeutic purposes.

Claim 29 (withdrawn): The method of Claim 28 wherein said cellular preparation of Step b. is genetically modified to deliver a therapeutic compound useful in the treatment of disease or the promotion of tissue repair.

Claim 30 (withdrawn): A method for the preparation of tissue useful for repair of tissues or organs in a host, said method comprising:

- a. preparing said tissue as in Claim 29; and
- b. implanting said tissue at the desired site for tissue or organ repair.

Claim 31 (currently amended): The device of Claim 1 wherein said cellular preparation comprises cells taken from ~~said host~~ and individual organism into whom the device and/or first and second layers of cells are to be implanted.

Claim 32 (currently amended): The device of Claim 8 wherein said cellular preparation comprises cells from the tissues adjacent to the intended site of ~~[[the]]~~ implant ~~[[of]]~~ for the device, that grow along said ~~platform surface~~ substrate.

Claim 33 (original): The device of either of Claims 1 or 8 wherein said substrate is bioresorbable.

Claim 34 (original): The device of either of Claims 1 or 8 wherein said substrate is flexible.

Claim 35 (original): The device of either of Claims 1 or 8 wherein said cells comprise cells of the nervous system.

Claim 36 (currently amended): The device of Claim 35 wherein said cells are derived from the central nervous system or "CNS".

Claim 37 (currently amended): The device of Claim 35 wherein said cells are selected from the group consisting of neurons, glial cells, astrocytes, microglial cells, and dorsal root ganglion (DRG) cells.

Claim 38 (new): The device of claim 8, further comprising three or more layers of cells, the third and greater layers of cells comprising organized layers of later-deposited cells oriented in the direction of the first and second layers.

Appl. No. 10/075,129  
Amdt. dated June 13, 2005  
Reply to Office Action of December 13, 2004.

Claim 39 (new): The device of claim 8, further comprising three or more layers of cells, the third and greater layers of cells comprising organized layers of later-deposited cells oriented in the direction of the first and second layers.